

NVI 5183.1
PATENT

REMARKS

Claims 1, 4-30, 113-116, 118-119, and 136-146, 148-150, and 153-154 are currently pending. Claims 144 and 145 have been withdrawn as directed to a non-elected invention. No claims have been amended.

I. Rejections under 35 U.S.C. §102(a) (Conkle, et al.)

Reconsideration is respectfully requested of the rejection of claims 1, 4-22, 29-30, 113-116, 118-119, 136-142, 146, 148-150, and 153-154 under 35 U.S.C. §102(a) as anticipated by Conkle, et al. (WO 00/50072).

At the outset, it must be respectfully emphasized that the entire Office action is predicated on the erroneous premise that that claim 1 fails to specify a structural difference from the Conkle, et al. and Evans, et al. references. Claim 1, and indeed each pending claim, expressly requires that that the composition be "substantially free of bacterial contaminants."¹ This is not only a structural difference, but a highly important structural difference from the teachings of both Conkle, et al. and Evans, et al.; not a mere "intended use." Once this is appreciated, it is respectfully submitted that the entire basis for the various prior art rejections falls away.

The extent of the freedom from bacterial contaminants is expressed in product-by-process language because it has not been quantified and thus cannot be expressed in terms of a numerically defined concentration. However, even as expressed in product-by-process language, the extent of freedom from bacterial contaminants comprises a further structural limitation; and such further structural limitation must also

¹Claim 1 reads as follows: "A composition for the prevention or control of coccidiosis comprising viable sporulated oocysts that are derived from an oocysts source comprising bacterial contamination and comprise at least one species of protozoa known to cause coccidiosis, wherein said composition is sterile and contains at least about 10,000 oocysts per milliliter and less than about 0.4% by weight of alkali metal dichromate, said composition being substantially free of bacterial contaminants which are present in said source but have been separated from said oocysts by tangential flow filtration of an aqueous process medium containing said oocysts and said bacterial contaminants using a filter membrane having a pore size such that sporulated oocysts cannot enter the pores, but said bacterial contaminants can pass through the pores."

NVI 5183.1
PATENT

be considered in evaluating the novelty and patentability of the claims. As stated in the MPEP:

The structure implied by the process steps should be considered when assessing the patentability of product-by-process claims over the prior art, especially where the product can only be defined by the process steps by which the product is made, or where the manufacturing process steps would be expected to impart distinctive structural characteristics to the final product.²

In the instant case, as noted, a structural limitation on bacterial contamination is expressly imposed by claim 1. More particularly, claim 1 requires the presence of oocysts that have been obtained from a source which contains bacterial contaminants, as is normally if not universally the case. The claim further characterizes the composition as:

"being substantially free of bacterial contaminants which are present in said source but have been separated from said oocysts by tangential flow filtration of an aqueous process medium containing said oocysts and said bacterial contaminants..."

In addition, Applicants submit that a "distinctive structural characteristic" is imparted by the specified requirement of tangential flow filtration using:

"a filter membrane having a pore size such that sporulated oocysts cannot enter the pores, but said bacterial contaminants can pass through the pores"

Thus, both the express substantial exclusion of "bacterial contaminants which are present in said source" and the product-by-process limitations impose a structural limitation on the claim.

By substantially excluding bacterial contaminants derived from the source of oocysts, it is respectfully submitted that claim 1 distinguishes the teachings of Conkle, et al. under 35 U.S.C. §102. It is recognized that Conkle, et al. teach the treatment of their

² MPEP §2113 (emphasis added).

NVI 5183.1
PATENT

compositions with antibacterial agents such as hydrogen peroxide or sodium hypochlorite. However, it is important to understand that "bacterial contaminants," as specified in claim 1 encompass not only live bacteria, but non-viable contaminants such as dead bacteria and cellular debris that remain after treatment with a anti-bacterial agent. Treatment according to Conkle, et al. may be effective for killing bacteria, but Conkle, et al. fail to teach or suggest removal of non-viable bacteria or bacterial debris, whether by tangential flow filtration or otherwise. Thus, the claim structurally distinguishes the vaccines of Conkle, et al. in this regard.

As specified in claim 1, since the pore size of the filter membrane used during tangential flow filtration is large enough to allow bacteria to pass through, the oocysts retained by the filter membrane have been separated from both viable and non-viable contaminants, such as bacteria and cellular debris. The oocysts in the composition of claim 1 thus contain a much lower amount of bacterial contaminants (both viable and non-viable) than would be present were the pore size small enough to retain bacteria as well as oocysts.

Conkle et al. particularly fail to disclose or suggest an oocyst-containing composition that is substantially free of bacterial contaminants that are present in a source but that have been separated from the oocysts by tangential flow filtration of an aqueous process medium containing the oocysts and the bacterial contaminants using a filter membrane with a pore size small enough to prevent sporulated oocysts from entering the pores, but large enough to allow bacteria to pass through the pores.

For example, Conkle, et al. state that oocysts may be washed following sporulation to reduce the residual oxidant concentration to an acceptable level. Serial washings may be conducted, preferably by membrane filtration, and more preferably by diafiltration. Serial washing or diafiltration may also be used after bleaching to reduce

NVI 5183.1
PATENT

the residual oxidant concentration in the bleached suspension (e.g., the concentration of sodium hypochlorite in the suspension), to an acceptable level.³

It is important to understand that the washing steps of Conkle, et al. do not render the Conkle, et al. vaccine "substantially free of bacterial contaminants." Significantly, Conkle, et al. fail to disclose or suggest the use of a filter pore size small enough to prevent sporulated oocysts from entering the pores, but large enough to allow bacteria to pass through the pores. Rather, the only mention in Conkle, et al. of pore size is a statement that in the case of membrane filtration, "the membrane pore size is selected to allow passage of solutes through the membrane while restricting the passage of the oocysts from one side of the membrane to the other."⁴ There is no statement or suggestion in Conkle, et al. that the pore size should also be large enough to allow the passage of bacteria, as well as solutes. In fact, such a pore size would not be necessary to achieve the stated purpose of washing in Conkle, et al., i.e., to reduce the residual oxidant concentration to an acceptable level. There is no suggestion of the desirability of separating the oocysts from bacterial or other contaminants that may be present in the sporulation medium, or in the bleached oocyst suspension. Consequently, in contrast to the composition of amended claim 1, the oocyst-containing compositions of Conkle, et al. are not, either expressly or inherently, substantially free of bacterial contaminants which are present in a source but have been separated from the oocysts by tangential flow filtration of an aqueous process medium containing the oocysts and the bacterial contaminants (including non-viable bacterial contaminants) using a filter membrane having a pore size such that sporulated oocysts can not enter the pores, but bacteria can pass through the pores.

³ "Following bleaching, the bleached suspension is washed, if necessary, to reduce the residual oxidant concentration to an acceptable level." Conkle, et al., p. 8, ln. 33-35.

⁴ Conkle, et al., p. 8, ln. 19-20 (emphasis added).

NVI 5183.1
PATENT

In the paragraph at the top of p. 7 of the Office action, the Examiner quotes Conkle's teaching that the encysted protozoa which include cysts and oocysts may be obtained from various sources including "purified suspension, intestinal linings and fecal suspensions." Presumably, the Examiner is not relying on the reference to "purified suspensions" as teaching the elimination of bacterial contaminants from the oocysts. If so, such reliance would be entirely misplaced. Conkle, et al. offer no explanation whatsoever as to what is meant by "purified suspension." It could mean almost anything, e.g., that the suspension has been treated with sodium hypochlorite. In any case, there is no disclosure in Conkle, et al. which remotely supports an inference that such suspensions are substantially free of bacterial contaminants including dead bacteria and cellular debris.

The composition of Conkle, et al. thus can be said to comprise a greater amount of non-viable bacterial contaminants than the composition of claim 1. Therefore, Conkle, et al. manifestly fail to describe each and every element of claim 1.

In response to applicants' arguments, the Office has stated that "the purification or production of a product by a particular process does not impart novelty or unobviousness to a product when the same product is taught by the prior art," (emphasis in original), and that "[t]his is particularly true when the properties of the product are not changed by the process in an unexpected manner."

But, as explained above in detail, the premise of this argument fails because here the "same product" is not taught by the prior art. As stated in MPEP §2131, a claim is anticipated under 35 U.S.C. §102 only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. For the reasons discussed above, Conkle, et al. fail to describe each and every element of claim 1, and therefore do not anticipate claim 1.

NVI 5183.1
PATENT

The authorities cited by the Examiner, i.e., *In re Thorpe*,⁵ *In re Marosi*,⁶ and *In re Brown*,⁷ are not to the contrary. They involve rejections of product-by-process claims under §102 where the applicant(s) had failed to identify any structural difference from the prior art, backed up by rejections under §103 on the basis that, if there were any structural differences, they were "slight." But none of these authorities supports either of the propositions for which they are cited in the Office action, i.e., none of these cases supports either: (i) the contention that a purified composition lacks novelty over a corresponding unpurified composition; or (ii) the suggestion that "unexpected properties" are required for novelty.

With regard to the Office's comments on purity, Applicants direct the Office's attention to MPEP §2144.04, which states:

Pure materials are novel vis-à-vis less pure or impure materials because there is a difference between pure and impure materials. Therefore the issue is whether claims to a pure material are unobvious over the prior art.

See also *In re Bergstrom*, 427 F.2d 1394, 166 USPQ 256 (CCPA 1970) where the PTO had rejected claims to certain pure prostaglandin compounds for lack of novelty in light of the material from which it was extracted. On appeal, the court held:

We need not decide the merits of that matter, for the fundamental error in the Board's position, as we see it, is the analysis and answer it gave to the sole issue it accurately posed -- 'whether the *claimed* pure materials are *novel* as compared to the *less pure* materials of the reference'...It seems to

⁵227 USPQ 964 (Fed. Cir. 1985).

⁶218 USPQ 289 (Fed. Cir. 1983).

⁷173 USPQ 685 (C.C.P.A. 1972).

NVI 5183.1
PATENT

us that the answer to that question is self-evident: by definition, pure materials necessarily differ from *less* pure or impure materials...⁸

Applicants thus submit that claim 1 is patentable under 35 U.S.C. §102 over Conkle, et al.

A. Patentability over Conkle, et al. under 35 U.S.C. §103(a), "Unexpected Properties"

Although the Office action still contains no express obviousness rejection over Conkle alone, it continues to make arguments that relate to obviousness under §103 rather than novelty under §102. In this category is the contention that a showing of "unexpected properties" is necessary to establish novelty. Contrary to the Examiner's assertion, novelty requires nothing unexpected, only that the claimed subject matter differs from what can be found in the four corners of any single reference.

"Unexpected properties" is an issue which can arise in the context of obviousness. Unexpected properties are not a requirement for non-obviousness; but they can be relevant as secondary evidence overcoming a rejection for *prima facie* obviousness as made under the three part inquiry mandated by *Graham v. John Deere*, 383 U.S. 1 (1966).

In the instant application, the Examiner has neither entered a rejection under §103(a) based on Conkle alone nor offered any basis for *prima facie* obviousness of a coccidiosis vaccine which is substantially free of bacterial contaminants. In the absence of *prima facie* obviousness, there is no burden on applicants to offer secondary evidence of any sort, whether by commercial success, failure of others, unexpected properties, or otherwise.

However, since the subject of unexpected properties has been raised, it nevertheless may be helpful to point out that the properties of the claimed vaccine are

⁸*Bergstrom*, 166 USPQ at 262 (emphasis added by court).

NVI 5183.1
PATENT

indeed unexpected when considered in light of Conkle, et al. Conkle, et al. neither describe a vaccine which is substantially free of bacterial contamination, nor suggest that there is any need for such a vaccine, nor suggest any way to accomplish such results. Thus, Conkle, et al. create no basis for one skilled in the art to expect that a coccidiosis vaccine comprising oocysts but substantially free of bacterial contaminants might be provided, or could feasibly be provided, or would serve any purpose if it were provided. Only with the hindsight afforded by applicants' invention can it be seen that there is any need or purpose to provide a vaccine free of bacterial contaminants that include dead bacteria and cellular debris. And only with the hindsight afforded by applicants teachings can it be seen that such a vaccine can feasibly be provided, that it can be produced by tangential flow filtration using a membrane of a certain pore size, and that it provides the important advantage of being less susceptible to creating pyrogenic reactions than the vaccine of Conkle. Thus, all claims should be deemed patentable under the authority of *In re Wakefield*, 422 F.2d 897, 164 USPQ 636 (CCPA 1970), in which a claim reciting "synthetic rubber" was held patentable over a disclosure of otherwise identical subject matter which comprised "natural rubber," despite the absence of any identified structural difference. As stated by Judge Lane:

We now turn to the examiner's view adopted by the Board, that the synthetic product is so similar to the natural product, purified to the extent allegedly shown in Davis, as to be '*prima facie* obvious.' We would agree with this conclusion as a tentative one based on similarity of structure and gross characteristics. However, such tentative conclusions of obviousness are rebutted in those instances where there was, at the time the invention was made, no known method or obvious method of making the claimed composition, or where the claimed composition is found to possess unexpected characteristics.⁹

⁹*Wakefield*, 422 F.2d at 903.

NVI 5183.1
PATENT

A fortiori, the vaccine of claim 1 herein should be found patentable where it recites definitive structural characteristics which distinguish it from Conkle, et al. where Conkle, et al. fail to suggest any method for producing the vaccine as defined in the claim, where reducing bacterial contamination reduces the the potential pyrogenicity, and where Conkle, et al. fail even to recognize the problem that can be caused by dead organisms and/or cellular debris or any need to deal with it.

In another passage that could be relevant only to a rejection for obviousness, the Examiner suggests a need for side by side comparison of the claimed vaccine with Conkle, et al. However, the need for such comparison could arise only if there were *prima facie* obviousness, which has not been shown. Even if *prima facie* obviousness had been shown, side by side comparison would be needed only if experimental evidence were necessary to establish a material difference from the prior art. Here the substantial absence of bacterial contamination is a material and unobvious difference, and flowing from that difference is an important difference in potential pyrogenicity.¹⁰

Claim 1 is thus patentable over Conkle, et al. under §102 and/or §103.

Claims 4-8, 14-22, 29-30, 113-116, 118-119, 136-142, 146, 148-150, and 153-154 depend either directly or indirectly from claim 1 and are thus patentable for the same reasons as set forth above for claim 1 as well as for the additional elements they require.

Claim 9 is similar to claim 1, except the composition comprises at least about 300 oocysts per milliliter and less than about 0.002% by weight of alkali metal dichromate. Claim 10 is similar to claim 1, except the composition comprises less than about 5.0×10^{-3} μ g of alkali metal dichromate per oocyst and has no limitation on the amount of oocysts

¹⁰The Office has stated that applicants' arguments with regard to pyrogenic reactions are tantamount to arguing limitations of intended use for the claimed product, and that a recitation of intended use must result in a structural difference between the claimed invention and the prior art in order to distinguish the prior art. Initially, applicants note that the composition of claim 1 is structurally different from the composition of Conkle, et al., for the reasons discussed above. Furthermore, it is this structural difference (e.g., a lower amount of non-viable bacterial contaminants) that provides the composition of claim 1 with an unexpected advantage over the compositions of Conkle, et al., i.e., a reduced risk that animals administered the composition will experience a pyrogenic reaction.

NVI 5183.1
PATENT

per milliliter. Claims 9 and 10, as well as claims 11-13 which depend either directly or indirectly from claim 10, are thus patentable for the same reasons as set forth above for claim 1, as well as for the additional elements they require.

B. Claim 113

Claim 113, directed to a kit comprising the composition of claim 1 and instructions for administration of the composition to an animal, depends from claim 1. Claim 113 is thus patentable for the same reasons as set forth above for claim 1 as well as for the additional elements it requires.

The Office has also reiterated its previous rejection of claim 113, stating that a package insert, such as instructions, does not lend patentable weight to the claim, absent a functional relationship between the instructions and the composition. The Office has further stated that the instructions are a limitation of intended use and if the composition of Conkle, et al. is capable of performing the intended use, then it meets the claim.

Applicants again respectfully submit that the instructions in the kit of claim 113 constitute more than a mere intended use; they are functionally related to the composition, and therefore should be given patentable weight.¹¹ Claim 113 is directed to a kit for the prevention or control of coccidiosis, comprising the composition and the instructions for administration of the composition to an animal; claim 113 is not directed to either the composition or instructions alone. Furthermore, the compositions of the present invention may be administered by a variety of routes, and may require dilution

¹¹ "Under section 103, the board cannot dissect a claim, excise the printed matter from it, and declare the remaining portion of the mutilated claim to be unpatentable. The claim must be read as a whole." *In re Gulack*, 217 USPQ 401, 403 (Fed. Cir. 1983). Furthermore, "[t]he fact that printed matter by itself is not patentable subject matter, because non-statutory, is no reason for ignoring it when the claim is directed to a combination." *In re Miller*, 164 USPQ 46, 49 (C.C.P.A. 1969).

NVI 5183.1
PATENT

before administration.¹² The instructions in claim 113 are for administration of the composition to an animal, and are thus functionally related to the composition since they allow the user of the kit to gain the additional benefit of a properly prepared and administered composition. Claim 113 is thus patentable under 35 U.S.C. §102 over Conkle, et al. for this additional reason.

Claims 114-116 and 118-119 depend directly or indirectly from claim 113 and are thus patentable for the same reasons as set forth above for claim 113 as well as for the additional elements they require.

C. Claim 139

The Office has also reiterated its rejection of claim 139, stating that the phrase "a ratio defined by the minimum immunizing dose and amount determined by storage [half]-life determinations" is inherent and is a limitation of intended use.

As discussed above, claim 139 depends indirectly on claim 1 and is thus patentable for the same reasons as set forth above for claim 1. It is respectfully submitted that the patentability of claim 139 is fully established on the same basis as claim 1, so that no further response is properly necessary.

In addition, however, applicants respectfully submit that the phrase "...a ratio defined by the minimum immunizing dose and amount determined by storage half-life determinations" is more than a mere limitation of intended use, and that it cannot be found inherently in Conkle, et al. based on the reference's general disclosure that encysted protozoa oocysts including *Eimeria maxima*, *E. mitis*, *E. tenella*, *E. acervulina*, *E. brunetti*, *E. necatrix*, *E. praecox*, and mixtures thereof can be given in a single vaccine.

¹² "The vaccine may be concentrated, requiring dilution before administration, or the vaccine may be ready for administration. The concentrated embodiment of the instant invention may be diluted with any suitable diluent to concentrations suitable for various forms of administration, including intra-yolk sac administration, per os, oral gavage, delivery via spray cabinet, or top-fed via spray onto food, such as OASIS Hatchling Supplement." Specification, p. 46, ln. 15-20.

NVI 5183.1
PATENT

The phrase "in a ratio defined by the minimum immunizing dose and amount determined by storage half-life determinations" does not specify any intended use of the composition as a whole, but instead quantifies the amounts of *E. acervulina*, *E. maxima*, and *E. tenella* sporulated oocysts and ratios thereof that are present in the composition.¹³ As such it is an entirely structural limitation. Since a certain number of sporulated oocysts cease to be functional as they age, providing a quantity of sporulated oocysts as defined by claim 139 helps to assure that quantity of viable oocysts will be sufficient for the vaccine to be effective when used. For this purpose, the minimum number of sporulated oocysts of each *Eimeria* species in the composition may be determined using the minimum immunizing dose and the storage half-life of the sporulated oocysts. As those skilled in the art will readily understand from Applicants' specification, the half life defines the slope of the logarithmic decay curve. Back projection on this curve over a period corresponding to storage life defines the amount of oocysts that must be contained in the original dose package in order to assure that minimum immunizing dose remains on the day of administration.¹⁴

The Office has again provided no evidence whatsoever to support its stated conclusion that the claim limitation "a ratio defined by the minimum immunizing dose and amount determined by storage half-life determinations" is inherent in Conkle, et al. To establish inherency, "the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent

¹³ "The combined species of sporulated oocysts are present in a number sufficient to comprise the minimum number of sporulated oocysts required to comprise an effective dose for immunizing purposes." Specification, p. 45, ln. 18-21.

¹⁴ "The number of sporulated oocysts per dose is further determined by the estimated half-life of the sporulated oocysts in the storage composition claimed herein. As the sporulated oocysts age a certain number cease to be functional...Therefore, a minimum amount of a single species or combination of sporulated oocysts is added to the compositions for consumption that will result in the minimum immunizing dose computed as a function of half-life determinations." *Id.* at ln. 21-27.

NVI 5183.1
PATENT

characteristic necessarily flows from the teachings of the applied prior art.¹⁵ "The fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic."¹⁶ The Office has provided no such basis. In response to applicants arguments, the Office merely makes the general statement: "Vaccines are known as pharmaceutical compositions that are used to immunize subjects and are thereby given in immunizing doses and can include determination by storage half-life determinations."

However, Conkle, et al. do not describe any ratio of *E. acervulina*, *E. maxima*, and *E. tenella* sporulated oocysts present in their composition. As previously discussed, Conkle, et al. merely state that the coccidial oocysts can be *E. maxima*, *E. mitis*, *E. tenella*, *E. acervulina*, *E. brunetti*, *E. necatrix*, *E. praecox*, and mixtures thereof, but do not disclose or suggest any ratio of oocysts. Furthermore, Conkle, et al. do not discuss the problem of aging of sporulated oocysts during shipping and storage, much less how to determine a suitable amount of oocysts by storage half-life determinations. Consequently, the compositions of Conkle, et al. cannot be said to *necessarily* comprise sporulated oocysts of *E. acervulina*, *E. maxima*, and *E. tenella* in a ratio defined by the minimum immunizing dose and amount determined by storage half-life determinations, as required by claim 139. Conkle, et al. can thus not be said to describe all the limitations of claim 139, and claim 139 is thus also patentable for this further reason.

Moreover, the Examiner's contention that pharmaceutical compositions administered in immunizing doses "can include determination by storage half life determinations" is undocumented by any source other than applicant's specification. And even if the proposition stated by the Examiner were accepted as known art, it does

¹⁵ MPEP § 2112 (citing *Ex parte Levy*, 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990) (emphasis in original)).

¹⁶ MPEP §2112 (citing *In re Rijckaert*, 9 F.3d 1531, 1534 (Fed. Cir. 1993)). MPEP §2112 also states "[i]nherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient." (quoting *In re Robertson*, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999)).

NVI 5183.1
PATENT

not meet the requirement of claim 139 that "sporulated oocysts of *Eimeria acervulina*, *Eimeria maxima*, and *Eimeria tenella*" are present "in a ratio defined by the minimum immunizing dose and amount determined by storage half-life determinations."

In light of the foregoing, applicants respectfully request withdrawal of the rejection of claims 1, 4-22, 29-30, 113-116, 118-119, 136-142, 146, 148-150, and 153-154 under 35 U.S.C. §102, and allowance of these claims.

II. Rejections under 35 U.S.C. §103(a) (Conkle, et al. and Brown, et al.)

Reconsideration is further requested of the rejection of claims 1, 4-30, 113-116, 118-119, 136-143, 146, 148-150, and 153-154 under 35 U.S.C. §103(a) as unpatentable over Conkle, et al. (WO 00/50072), in view of Brown, et al. (U.S. Patent No. 6,019,985).

Brown, et al. is apparently relied on primarily as suggesting the incorporation of *P. acnes* into the compositions of Conkle, et al. However, other than the disclosure of *P. acnes*, Applicants are unable to identify anything which Brown, et al. add to the teachings of Conkle, et al. Nor has the Examiner identified any other teaching of Brown, et al. that is relevant to the compositions as claimed herein. Thus, citation of the Brown, et al. reference would appear to have relevance only with respect to claims 23-28, 142, and 143, which call for a component composition which ameliorates a decline in post-challenge performance, and specifically to claims 26-28 and 143 which expressly call for the presence of *P. acnes*.

In any event, Applicants respectfully submit that all claims are patentable over Conkle et al., and over any combination of Conkle, et al. and Brown, et al. under §103.¹⁷

As explained above, the express exclusion of "bacterial contaminants which are present in said source" and the product-by-process limitations in claim 1 impose

¹⁷To whatever extent the Examiner may have intended to reject claims 1, 4-22, 29, 30, 113-113, 118-119, 136-141, 146, 148-150, and/or 153-154 under §103(a) based on Conkle, et al. alone, such ground of rejection is dealt with in Part I of this response, more particularly in Part I(A), pages 8-11, as further elaborated below in response to the §103(a) rejection over Conkle, et al. in view of Brown, et al.

NVI 5183.1
PATENT

structural limitations on the claim that distinguish it from the cited references. In particular, the composition of claim 1 comprises a lower amount of non-viable bacterial contaminants than the composition of Conkle, et al. alone, or in combination with the *P. acnes* described in Brown, et al. Since there is no disclosure or suggestion in either Conkle, et al. or in Brown, et al. (nor any motivation to modify the cited references) of oocyst containing compositions that are substantially free of bacterial contaminants which are present in a source but have been separated from the oocysts by tangential flow filtration of an aqueous process medium containing the oocysts and the bacterial contaminants using a filter membrane having a pore size such that sporulated oocysts cannot enter the pores, but the bacterial contaminants can pass through the pores, the cited references fail to teach or suggest all the limitations of claim 1.

Furthermore, there is no statement or suggestion in either of the cited references of the desirability of separating oocysts from non-viable bacterial or other contaminants that may be present in the composition or during processing. As discussed above, Conkle, et al. disclose washing oocysts following sporulation to reduce the residual oxidant concentration to an acceptable level. There is no recognition in Conkle, et al. of the desirability of producing a composition with a reduced amount of non-viable bacterial contaminants nor any suggestion as to how such a composition could be produced. There is likewise no such recognition in Brown, et al., which merely discloses administering *P. acnes* to chicks in ovo or following hatching. Brown, et al. state that hatched chicks may also be administered an anti-coccidial vaccine in combination with the *P. acnes*, but do not disclose anything about dosage, or for that matter anything about the composition of the vaccine beyond the fact that it contains "killed or weakened pathogenic microorganisms." Brown does not suggest removing any non-viable bacterial contaminants from the vaccine, much less reducing them to the level that is achieved by tangential flow filtration as defined in applicants' claims.

In addition, as discussed above, the composition of claim 1 provides an advantage over other compositions (such as the composition of Conkle, et al. alone or in

NVI 5183.1
PATENT

combination with the *P. acnes* of Brown, et al.) in that the lower amount of non-viable bacterial contaminants reduces the risk that animals administered the composition will experience a pyrogenic reaction. Applicants thus submit that the composition of claim 1 has an unexpected and unique property (in this instance freedom from an adverse side effect inherent in the compositions of the cited references) that further distinguishes it from the compositions disclosed in the cited references.

In light of the foregoing, Applicants respectfully submit that claim 1 is patentable over Conkle, et al. and Brown, et al., either alone or in combination.

Claims 4-8, 14-30, 113-116, 118-119, 136-143, 146, 148-150, and 153-154 depend either directly or indirectly from claim 1 and are thus patentable for the same reasons as set forth above for claim 1 as well as for the additional elements they require.

Claims 9 is similar to claim 1, except the composition contains at least about 300 oocysts per milliliter and less than about 0.002% by weight of alkali metal dichromate. Claim 10 is similar to claim 1, except the composition contains less than about 5.0×10^{-3} μ g of alkali metal dichromate per oocyst and has no limitation on the amount of oocysts per milliliter. Claims 9 and 10, as well as claims 11-13 which depend either directly or indirectly from claim 10, are thus patentable for the same reasons as set forth above for claim 1, as well as for the additional elements they require.

A. Claims 23 and 142

Claims 23 and 142 are indirectly dependent on claim 1, and are thus patentable for the same reasons as set forth above for claim 1. Furthermore, the Office has appeared to misinterpret claims 23 and 142. The Office has stated that "[c]laim limitations such as...'the composition ameliorates a decline in post-challenge performance' ... are being viewed as limitations of intended use."

Claim 23 (dependent on claim 14) and claim 142 (dependent on claim 137) are directed to compositions which further comprise, as a component thereof, a composition which ameliorates a decline or decrease in post-challenge performance (i.e. an

NVI 5183.1
PATENT

ameliorating composition).¹⁸ The phrase "which ameliorates a decrease [or decline] in post-challenge performance" does not specify a mere property of the composition as a whole, but instead defines an additional component of that composition by a functional characteristic which that component possesses. Such "ameliorating composition" is a component that is included in the sporulated oocyst-containing compositions of claims 14 and 137, respectively, to provide the compositions claimed in claims 23 and 142. The phrase "which ameliorates a decrease [or decline] in post-challenge performance" thus does not refer to a mere intended use, but rather, to an ameliorating composition which is a component of the composition of claims 23 and 142.

III. Rejections under 35 U.S.C. §102(b) (Evans, et al.)

Reconsideration is requested of the rejection of claims 1, 4-22, 29-30, 113-116, 118-119, 136-142, 146, 148-150, and 153-154 under 35 U.S.C. §102(b) as anticipated by Evans, et al. (WO 96/40234).

Applicants submit that Evans, et al. do not disclose, either expressly or inherently, each and every element of claim 1. For the reasons set forth above, applicants again submit that the express exclusion of "bacterial contaminants which are present in said source" and the product-by-process limitations in claim 1 impose structural limitations on the claim that distinguish it from the cited reference. In particular, the oocysts in the composition of claim 1 contain a much lower amount of both viable and non-viable bacterial contaminants than would be present were the pore size used during tangential flow filtration small enough to retain bacteria as well as oocysts.

By substantially excluding bacterial contaminants derived from the source of oocysts, it is respectfully submitted that claim 1 distinguishes the teachings of Evans, et al. under 35 U.S.C. §102(b) on this ground. In particular, Evans, et al. fail to disclose or suggest a sporulated oocyst-containing composition that is substantially free of bacterial

¹⁸ See Specification, p. 44 for a description of compositions which ameliorate a decrease in post challenge performance.

NVI 5183.1
PATENT

contaminants that are present in a source but that have been separated from the oocysts by tangential flow filtration of an aqueous process medium containing the oocysts and the bacterial contaminants using a filter membrane with a pore size small enough to prevent sporulated oocysts from entering the pores, but large enough to allow bacteria to pass through the pores.

For example, Evans, et al. state that repeated washings, which involve collection of oocysts by centrifugation and resuspending in deionized or distilled water, may be used to remove the potassium dichromate from the oocyst suspension. Repeated washings may also be used to remove sodium hypochlorite from the oocysts.¹⁹ Such washings would not, however, remove non-viable contaminants from the compositions.²⁰ Significantly, Evans, et al. do not even disclose the use of tangential flow filtration, much less the use of a filter pore size small enough to prevent sporulated oocysts from entering the pores, but large enough to allow bacteria to pass through the pores. Nor is there any suggestion of the desirability of separating the oocysts from non-viable bacterial or other contaminants that may be present in the oocyst suspension. Consequently, any composition of Evans, et al. that comprises sporulated oocysts would not, either expressly or inherently, be substantially free of bacterial contaminants which are present in a source but have been separated from the oocysts by tangential flow filtration of an aqueous process medium containing the oocysts and the bacterial contaminants (including non-viable bacterial contaminants) using a filter membrane having a pore size such that sporulated oocysts can not enter the pores, but bacteria can pass through the pores. Any composition of Evans, et al. that comprises sporulated

¹⁹ See Evans, et al., p. 6, lines 6-7.

²⁰ Applicants note that the centrifugation of an oocyst suspension followed by resuspending in water will not remove non-viable bacterial contaminants to the extent the tangential flow filtration described in claim 1 does. In particular, in the washing described by Evans, et al., non-viable contaminants will be "collected" along with the oocysts during centrifugation, or in any case Evans, et al. fail to disclose centrifugation conditions that would conceivably be effective to retain bacterial contaminants in the centrate. Thus, when the oocysts are resuspended, the non-viable contaminants will be carried over into the "washed" composition.

NVI 5183.1
PATENT

oocysts can thus be said to comprise a greater amount of non-viable bacterial contaminants than the composition of claim 1.

The Office has again stated that "the purification or production of a product by a particular process does not impart novelty or unobviousness to a product when the same product is taught by the prior art," and has required applicants to show an unexpected property of the claimed product, such as freedom from some restrictive element or adverse side effects inherent in the product of the prior art. But, as explained above, the premise of this argument fails because here the "same product" is not taught by the prior art. Thus, contrary to the Office's assertion, applicants are not required to show any unexpected property of the claimed composition to overcome the instant novelty rejection.²¹ Since, Evans, et al. fail to describe each and every element of claim 1, Evans, et al. do not anticipate claim 1.

In addition, Evans, et al. do not disclose a composition comprising viable sporulated oocysts in an amount of at least about 10,000 oocysts per milliliter²² and less than about 0.4% by weight of alkali metal dichromate. With regard to dosage, the Office action states that Evans, et al. teach that a typical dose of sporulated oocysts is 200,000 oocysts/bird. Applicants note that this is not the amount of oocysts in the compositions of Evans, et al., but rather is the dose of oocysts used to infect commercial broiler chickens with the *Eimeria* species of interest. The oocysts used to prepare the sporozoite and/or merozoite composition of Evans, et al. are then harvested from feces

²¹As noted above, a showing of "unexpected properties" is not necessary to establish novelty, but, rather, can be used as secondary evidence to overcome a rejection for *prima facie* obviousness. Since the Office has neither entered a rejection under §103(a) based on Evans, et al. alone nor offered any basis for *prima facie* obviousness of a coccidiosis vaccine comprising sporulated oocysts which is substantially free of bacterial contaminants, there is no burden on applicants to offer secondary evidence.

²²The Office has stated that Evans, et al. teach that a typical dose of sporulated oocysts is 200,000 oocysts/bird. Applicants note that this is not the amount of oocysts in the compositions of Evans, et al., but rather is the dose of oocysts used to infect commercial broiler chickens with the *Eimeria* species of interest. The oocysts used to prepare the sporozoite and/or merozoite composition of Evans, et al. are then harvested from feces of the infected birds. See Evans, et al., page 5, lines 15-20.

NVI 5183.1
PATENT

of the infected birds. See Evans, et al., page 5, lines 15-20. Evans, et al. also fail to teach that their compositions comprise less than about 0.4% by weight of alkali metal dichromate. Evans, et al. sporulate the oocysts by suspending them in a potassium dichromate solution (2.5% w/v) and incubating the resulting suspension with shaking.²³ Prior to preparing sporocysts, potassium dichromate is removed from the oocysts "by repeated washings of the oocysts, which involves collection of oocysts by centrifugation and resuspending in deionized or distilled water." The removal of dichromate is judged by the lack of a yellowish-orange coloration in the suspension.²⁴ There is, however, no disclosure of the concentration of potassium dichromate remaining in the oocyst suspension after washing.

The Office has stated that the disclosure in Evans, et al. of repeatedly washing the oocysts to remove potassium dichromate constitutes a teaching of "less than about 0.4% by weight of alkali metal dichromate." Applicants respectfully disagree. Since Evans et al. offer no express teaching of the level to which the potassium dichromate content is or should be reduced, the Office action is necessarily asserting that a level <0.4 wt.% is inherent in Evans. However, as explained above, to establish inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied art. The fact a certain result may occur is not sufficient. Here the Office action includes no attempt to offer evidence or reasoning supporting the conclusion that the washing steps described by Evans would inevitably and invariably provide a potassium dichromate content less than about 0.4 wt.%.

- With regard to the ultimate potassium dichromate content, it may be noted that Evans et al. fail to specify any of a variety of variables that would affect the result. For example, there is no disclosure regarding either: (i) the volume of wash water relative to

²³Evans, et al., page 5, lines 26-28.

²⁴*Id.* at p. 6, lines 1-5.

NVI 5183.1
PATENT

the amount of oocysts washed; (ii) the number of washes; (iii) the type of centrifuge employed; (iv) the speed or diameter of the centrifuge, or the centripetal force or acceleration generated thereby; (v) the centrifugation cycle; (v) the cake wetness; (vi) the density or viscosity of the liquid phase; etc. etc. In the absence of such quantitative information, there can be no basis for any conclusion that the potassium dichromate content is reduced to any particular residual level.

As to the Office's comments regarding purity, the phrase "the composition ameliorates a decline or decrease in post-challenge performance," the phrase "a ratio is defined by the minimum immunizing dose and amount determined by storage [half]-life determinations," and kits and package inserts, applicants refer to the arguments made above with respect to Conkle, et al., and submit that a similar line of reasoning applies in the context of the Evans, et al. reference.

Evans, et al. thus manifestly fails to describe each and every element of claim 1. Applicants thus submit that claim 1 is patentable under 35 U.S.C. §102(b) over Evans, et al.

Claims 4-8, 14-22, 29-30, 113-116, 118-119, 136-142, 146, 148-150, and 153-154 depend either directly or indirectly from claim 1 and are thus patentable for the same reasons as set forth above for claim 1 as well as for the additional elements they require.

Claim 9 is similar to claim 1, except the composition contains at least about 300 oocysts per milliliter and less than about 0.002% by weight of alkali metal dichromate. Claim 10 is similar to claim 1, except the composition contains less than about 5.0×10^{-3} μ g of alkali metal dichromate per oocyst and has no limitation on the amount of oocysts per milliliter. Claims 9 and 10, as well as claims 11-13 which depend either directly or indirectly from claim 10, are patentable for the same reasons as set forth above for claim 1.

A. Claims 6, 116, 136

NVI 5183.1
PATENT

Claims 6, 116, and 136 all depend directly or indirectly from claim 1, and are thus patentable for the same reasons as set forth above for claim 1. In addition, these claims are directed to either a composition (claims 6 and 136) or a kit comprising a composition (claim 116) that is substantially free of alkali metal dichromate.

As stated in the specification, "the term substantially free of alkali metal dichromate indicates that no alkali metal dichromate is added to the composition during production, including the sporulation and storage of said composition."²⁵ However, as discussed above, Evans, et al. suspend the oocysts in potassium dichromate prior to sporulation. Consequently, Evans, et al. do not disclose compositions "substantially free of alkali metal dichromate" as that term is used in claims 6, 116, and 136. Claims 6, 116, and 136 are thus patentable over Evans, et al. for this additional reason.

In light of the foregoing, applicants respectfully request withdrawal of the rejection of claims 1, 4-22, 29-30, 113-116, 118-119, 136-142, 146, 148-150, and 153-154 under 35 U.S.C. §102(b) and allowance of these claims.

Rejections under 35 U.S.C. §103(a) (Evans, et al. and Brown, et al.)

Reconsideration is requested of the rejection of claims 1, 4-30, 113-116, 118-119, 136-143, 148-150, and 153-154 under 35 U.S.C. §103(a) as unpatentable over Evans, et al. (WO 96/40234) in view of Brown, et al. (U.S. Patent No. 6,019,985).

Brown, et al. is apparently relied on primarily as suggesting the incorporation of *P. acnes* into the compositions of Evans, et al. However, other than the disclosure of *P. acnes*, the Office has not identified any other teachings of Brown, et al. that is relevant to the compositions as claimed herein. Thus, applicants again note that citation of the Brown, et al. reference would appear to have relevance only with respect to claims 23-28, 142, and 143, which call for a component composition which ameliorates a decline in

²⁵Specification, p. 6, lines 3-5.

NVI 5183.1
PATENT

post-challenge performance, and specifically to claims 26-28 and 143 which expressly call for the presence of *P. acnes*.

In any event, applicants respectfully submit that all claims are patentable over Evans, et al., and over any combination of Evans, et al. and Brown, et al. under §103.

For the reasons set forth above, applicants again submit that the express exclusion of "bacterial contaminants which are present in said source" and the product-by-process limitations in claim 1 impose a structural limitation on the claim that distinguishes it from the cited references. In particular, the composition of claim 1 comprises a lower amount of non-viable bacterial contaminants than any sporulated-oocyst containing composition of Evans, et al. alone, or in combination with the *P. acnes* described in Brown, et al. Since there is no disclosure or suggestion in either Evans, et al. or in Brown, et al. (nor any motivation to modify the cited references) of oocyst containing compositions that are substantially free of bacterial contaminants which are present in a source but have been separated from the oocysts by tangential flow filtration of an aqueous process medium containing the oocysts and the bacterial contaminants using a filter membrane having a pore size such that sporulated oocysts cannot enter the pores, but the bacterial contaminants can pass through the pores, the cited references fail to teach or suggest all the limitations of claim 1.

Furthermore, there is no statement or suggestion in either of the cited references of the desirability of separating oocysts from non-viable bacterial or other contaminants that may be present in the composition or during processing. As discussed above, Evans, et al. disclose repeated washings, which involve collection of oocysts by centrifugation and resuspending in deionized or distilled water, to remove the potassium dichromate from the oocyst suspension or to remove sodium hypochlorite from the oocysts. There is no recognition in Evans, et al. of the desirability of producing a composition comprising sporulated oocysts that has a reduced amount of non-viable bacterial contaminants nor any suggestion as to how such a composition could be produced. There is likewise no such recognition in Brown, et al., which merely discloses

NVI 5183.1
PATENT

administering *P. acnes* to chicks in ovo or following hatching. Brown, et al. state that hatched chicks may also be administered an anti-coccidial vaccine in combination with the *P. acnes*, but do not disclose or suggest removing non-viable bacterial contaminants from the vaccine, much less how a composition with a reduced amount of non-viable bacterial contaminants could be produced.

In addition, as discussed above, the composition of claim 1 provides an advantage over other compositions (such as any sporulated oocyst containing composition of Evans, et al. alone or in combination with the *P. acnes* of Brown, et al.) in that the lower amount of non-viable bacterial contaminants reduces the risk that animals administered the composition will experience a pyrogenic reaction. Applicants thus submit that the composition of claim 1 has an unexpected and unique property (in this instance freedom from an adverse side effect inherent in the sporulated oocyst-containing compositions of the cited references) that further distinguishes it from the compositions disclosed in the cited references.

In light of the foregoing, Applicants respectfully submit that claim 1 is patentable over Evans, et al. and Brown, et al., either alone or in combination.

Claims 4-8, 14-30, 113-116, 118-119, 136-143, 146, 148-150, and 153-154 depend either directly or indirectly from claim 1 and are thus patentable for the same reasons as set forth above for claim 1 as well as for the additional elements they require.

Claims 9 is similar to claim 1, except the composition contains at least about 300 oocysts per milliliter and less than about 0.002% by weight of alkali metal dichromate. Claim 10 is similar to claim 1, except the composition contains less than about 5.0×10^{-3} μ g of alkali metal dichromate per oocyst and has no limitation on the amount of oocysts per milliliter. Claims 9 and 10, as well as claims 11-13 which depend either directly or indirectly from claim 10, are thus patentable for the same reasons as set forth above for claim 1.

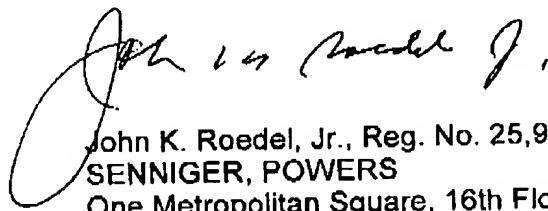
NVI 5183.1
PATENT

CONCLUSION

In light of the foregoing, applicants respectfully request withdrawal of the rejection of claims 1, 4-30, 113-116, 118-119, 136-143, 146, 148-150, and 153-154 and allowance of all claims.

The Commissioner is hereby authorized to charge any fees due in connection with this response, to Deposit Account No. 19-1345.

Respectfully submitted,


John K. Roedel, Jr., Reg. No. 25,914
SENNIGER, POWERS
One Metropolitan Square, 16th Floor
St. Louis, Missouri 63102
(314) 231-5400

JKR/LJH/